

### **DETAILED ACTION**

1. Claims 1-5, 8, 10-25, 28-31, 33-34, 36-43, 46-49, 96-99, 104-108, 110-114, 116-127, 129 and 131-133 are pending.
2. In view of the claims amendment filed February 26, 2009, the rejection of claims 25, 29, 31, 33-34, 36 and 37 under 35 U.S.C. 102(b) as being anticipated by US Pat No 5,693,762 B1 (newly cited issued Dec 2, 1997; PTO 892) has been obviated.
3. The rejection of claims 25 and 29-31 under 35 U.S.C. 102(b) as being anticipated by US Pat No 5,558,564 (of record, issued Sept 1996; PTO 892) has been obviated by the claims amendment filed February 26, 2009.
4. The rejection of claims 25, 28, 29, 31, 33-34, 36 and 37 under 35 U.S.C. 102(e) as being anticipated by US Pat No 6,884,879 (of record, filed August 6, 1997; PTO 892) as evidenced by US Pat No 5,693,762 B1 (newly cited issued Dec 2, 1997; PTO 892) has been obviated by the claims amendment filed and February 26, 2009.
5. The written description rejection of claims 1-5, 7-25, 28-34, 36-61, 63-74, 96-114, 116-127 and 129-133 under 35 U.S.C. 112, first paragraph has been obviated by the claims amendment filed February 26, 2009.

### **EXAMINER'S AMENDMENT**

6. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.
7. Authorization for this examiner's amendment was given in a telephone interview with Gregory P Einhorn on March 2, 2009.

Art Unit: 1644

8. **In the claims:**

- Claim 1, line 9, -- heavy chain -- has been inserted after "subgroup"
- Claim 1, lines 22-24 "(ii) expressing the substituted non-human antibody or antigen binding fragment thereof in the host cell, wherein the substituted non-human antibody" has been changed to -- (ii) expressing the non-human antibody or antigen binding fragment thereof having at least one substitution in the FR in the host cell, wherein the non-human antibody --
- Claim 3, line 2, "or" has been deleted.
- Claim 8 has been replaced with -- The method of claim 1, wherein the nucleic acid encoding the recombinant non-human antibody or antigen binding fragment thereof having at least one substitution in the FR is contained in an expression vector. --
- Claim 12, lines 3-4, "or the substituted non-human light chain variable domain having a substituted FR" has been deleted.
- Claim 19, line 6, "wherein" has been changed to -- are substituted with --
- Claim 19, last line, "are" has been deleted.
- Claim 25, line 8, -- heavy chain -- has been inserted before "variable"
- Claim 25, line 18, -- at least -- has been inserted before "one"
- Claim 25, line 20, "(a)(ii)" has been changed to -- (a)(iii) --
- Claim 25, line 22, "(a)(iii)" has been changed to -- (a)(ii) --
- Claim 25, lines 24-28, "wherein the substitution results in an antibody or antigen binding fragment thereof having an improved folding efficiency and yield when expressed in the host cell, and (b) expressing the substituted humanized antibody or substituted antigen binding fragment thereof in the host cell." has been changed to -- and (b) expressing said humanized antibody or antigen binding fragment thereof having at least one amino acid

Art Unit: 1644

substitution in the FR in the host cell wherein the substitution results in an antibody or antigen binding fragment thereof having an improved folding efficiency and yield. --

- Claim 33 has been rewritten as follow -- The method of claim 25, wherein the host cell comprises an expression vector comprising the nucleic acid sequence that encodes the non-human antibody or antigen binding fragment thereof having substitution in the FR. --
- Claim 34 has been rewritten as follow -- The method of claim 25, wherein the variable domain of the non-human antibody or antigen binding fragment thereof comprising the HVR1 and HVR2 and the selected FR substitution further comprises immunoglobulin constant domain to form a full-length heavy chain. --
- Claim 38, line 10, "position" has been deleted.
- Claim 39, line 3, -- heavy chain -- has been inserted after "subgroup"
- Claim 39, line 4, -- a heavy chain variable domain -- has been inserted after "a variable domain"
- Claim 39, line 6, -- heavy chain -- has been inserted after "subgroup"
- Claim 39, lines 10-11, "the framework" has been changed to -- the at least one framework --
- Claim 39, line 18, "substituted FR" has been changed to -- modified FR"
- Claim 39, line 19, "unsubstituted antibody" has been changed to -- unmodified antibody --
- Claim 39, lines 22-23, "substituted FR in the host cell and recovering the antibody or antigen binding fragment thereof with the substituted FR from the host cell." has been changed to -- modified FR in the host cell and recovering the recombinant antibody or antigen binding fragment thereof with the modified FR from the host cell. --
- Claim 41, line 3, "of" has been changed to -- from --
- Claim 42, line 3 "antibody" has been changed to -- an antigen --

Art Unit: 1644

- Claim 42, line 4 “positions 6 and 23” has been changed to -- positions 1, 6, 11, 13, 18, 19 and 23 --
- Claim 43, line 1-2, “positions 1, 6, 11, 13, 18, 19 and 23 of the heavy chain FR1 of SEQ ID NO: 3 are substituted.” has been changed to -- positions 6 and 23 of the heavy chain FR1 of SEQ ID NO: 3 are substituted with the corresponding amino acid found in SEQ ID NO: 1. --
- Claim 48, lines 4-5, "human variable domain subgroup sequence" has been changed to -- human subgroup heavy chain variable domain consensus sequence --
- Claim 49, line 2, “sequence” has been substituted with -- (FR) --
- Claim 96, lines 9-11, “(HVR2) sequence of the non-human variable domain of the antibody or antigen binding fragment thereof to corresponding HVR1 and/or HVR2 sequences of human subgroup variable domain consensus sequences,” has been changed to -- (HVR2) sequence of a heavy chain variable domain of the non-human antibody or antigen binding fragment thereof to corresponding HVR1 and/or HVR2 sequence of human subgroup heavy chain variable domain consensus sequences,”
- Claim 96, line 16, “recombinant” has been deleted.
- Claim 96, lines 17-18, “the substituted antibody or antigen binding fragment thereof” has been changed to -- said antibody or antigen binding fragment thereof having amino acid substitution in the FR --
- Claim 104, line 6, “human subgroup heavy chain variable domain consensus sequence" has been changed to -- human heavy chain subgroup variable domain consensus sequence --
- Claim 110 has been replaced with -- The method of claim 104, wherein the variable domain of the non-human antibody or antigen binding fragment thereof further comprises immunoglobulin constant region domain to form a full-length heavy chain. --

Art Unit: 1644

- Claim 112 has been replaced with -- The method of claim 111 further comprising recovering the full-length heavy chain or light chain from the cell or cell culture. --
  - Claim 127, line 2 “: (i)” has been deleted.
  - Claim 127, line 3, “, or (ii) deleted” has been deleted.
  - Claim 129, lines 14-15, “FR of the non-human variable domain of the antibody” has been changed to -- FR of the light chain variable domain of the non-human antibody --
  - Claim 129, lines 19-20, "substituted FR in the non-human variable domain of the antibody or antigen binding fragment thereof." has been changed to -- substituted FR in the light chain variable domain of the non-human antibody or antigen binding fragment thereof. --
9. Claims 1-5, 8, 10-25, 28-31, 33-34, 36-43, 46-49, 96-99, 104-108, 110-114, 116-127, 129 and 131-133 are allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh “NEON” whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O’Hara can be reached on (571) 272-0887. The IFW official Fax number is (703) 872-9306.
11. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Application/Control Number: 10/764,428

Page 7

Art Unit: 1644

/Phuong Huynh/

Primary Examiner, Art Unit 1644

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